**PRECLINICAL LAB STUDY
GRANT AGREEMENT
(Institution's IND)**

Grant Agreement, made this \_\_\_\_ day of \_\_\_\_\_, 1994, by and between THE UNIVERSITY OF TEXAS \_\_\_\_\_\_ (hereinafter referred to as "INSTITUTION"), a component institution of The University of Texas System (hereinafter referred to as "System"), located at \_\_\_\_\_\_\_ and Hoffmann-La Roche Inc., a subsidiary of [Hoffmann-La Roche Inc./Roche Laboratories], a New Jersey Corporation (hereinafter referred to as "ROCHE") located at 340 Kingsland Street, Nutley, New Jersey 07110-1199.

**WITNESSETH:**

WHEREAS, ROCHE is the manufacturer of \_\_\_\_\_\_\_\_\_\_\_\_ (hereinafter referred to as the "Compound"), which has potential utilization in the treatment of \_\_\_\_\_\_\_\_\_\_\_\_; and

WHEREAS, INSTITUTION has clinical situations which would allow evaluation and study of the Compound; and

WHEREAS, both ROCHE and INSTITUTION consider it necessary and desirable to better understand the effectiveness and use of said Compound and to accordingly complete the clinical evaluation of same;

NOW, THEREFORE, the parties agree as follows:

1. Evaluation. ROCHE agrees to engage the services of INSTITUTION to carry out the testing of the Compound as further described at Exhibit I. These evaluations will be at INSTITUTION with the assistance of appropriate associates and colleagues at INSTITUTION as may be required.

2. Principal Investigator/Sponsor. The Principal Investigator for the study shall be \_\_\_\_\_\_\_\_\_\_, who is also the Sponsor of the IND. The Principal Investigator/Sponsor shall be responsible for performing the study and the direct supervision of any individual performing portions of the study. In the event the Principal Investigator/Sponsor becomes unable to perform any of the activities in the study or complete the study for any reason, ROCHE and INSTITUTION may mutually agree to a substituted Principal Investigator/Sponsor, provided the new Agreement shall continue in full force and effect. INSTITUTION shall use its best efforts to identify and obtain a substitute Principal Investigator acceptable to ROCHE. If ROCHE and INSTITUTION cannot agree on a substitute Principal Investigator, or if a new IND is not obtained, ROCHE may immediately terminate this Agreement in accordance with Section 18.

3. Protocol. INSTITUTION agrees to conduct the evaluation according to the procedures described in Protocol \_\_\_\_\_ entitled "\_\_\_\_\_\_\_\_\_" attached as Exhibit I (the "Protocol") and incorporated herein by reference. INSTITUTION will conduct the Protocol as originally submitted and thereafter amended and approved in accordance with INSTITUTION policy and all applicable law.

4. Informed Consent. INSTITUTION agrees to obtain from each patient participating in the study the appropriate signed Informed Consent document as provided for in Exhibit I, and to retain such documents in accordance with policies of INSTITUTION and all applicable law.

5. Drug. ROCHE agrees to provide INSTITUTION with the required quantity of the Compound and investigational laboratory reagents as needed at no charge. INSTITUTION agrees to maintain control of the Compound in accordance with applicable law and standard procedure for investigational drugs and to return any unused quantities of such Compound at the conclusion of the evaluation in accordance with directions from ROCHE.

6. Result Forms. INSTITUTION will provide ROCHE with data obtained from the evaluation and result forms in accordance with the Protocol within sixty (60) days after each patient completion date or as requested by ROCHE and shall maintain all records as described in the Protocol.

7. Patent Rights.

(a) The work to be performed under this Agreement is the testing of the Compound supplied by ROCHE as specified in the Protocol. INSTITUTION may not use the Compound in any way other than as specified in the Protocol.

(b) If and only if any invention arises from the performance of this Agreement, this Section 7 shall apply. "Invention" shall mean any discovery, concept or idea, whether or not patentable, conceived and reduced to practice during the performance of this Agreement or conceived during the performance of this Agreement and reduced to practice within six (6) months after the expiration or termination of this Agreement, and resulting from performance of this Agreement in strict conformance with the Protocol. If required by the terms of an employment agreement, the inventor(s) shall assign patent rights to the Invention to his, her or their employer(s).

(1) Patent rights to an Invention made solely by employees of ROCHE shall belong to ROCHE. Institution shall not obtain any rights solely by having performed the study.

(2) Patent rights to an Invention made jointly by employees or agents of ROCHE and INSTITUTION shall be held jointly by ROCHE and INSTITUTION.

(3) INSTITUTION shall promptly notify ROCHE of any Invention and ROCHE shall have the rights set forth in subsection 7(b)(4) hereof.

(4) If the Principal Investigator and/or employee(s) of INSTITUTION alone are inventor(s), ROCHE and INSTITUTION shall negotiate the terms of a license to said Invention, and ROCHE shall have an exclusive option to negotiate an exclusive worldwide license of all rights to the Invention whether such rights are held by the Principal Investigator or the INSTITUTION. If ROCHE commercializes the Invention, ROCHE shall pay INSTITUTION a royalty for such license to be negotiated by the parties in good faith based upon the relative contribution to the Invention and the commercial value of the Invention. ROCHE shall inform INSTITUTION within sixty (60) days from the date of disclosure of the Invention by INSTITUTION whether it wishes to obtain a license. The parties shall not be obligated to negotiate for more than six (6) months from the date that ROCHE informs INSTITUTION that it wishes to secure a license, or such other reasonable period of time to which the parties may later agree to in writing. If the parties are unable to reach an agreement, ROCHE shall have a right of first refusal to accept any terms offered to a third party for rights to the Invention.

(5) In the event ROCHE and INSTITUTION have executed a license agreement covering any Invention pursuant to subsection 7(b)(4) hereof, appropriate U.S. and foreign patent applications for such Invention shall be filed by INSTITUTION, for Inventions on which it is the sole assignee. In the event INSTITUTION is making any filing, ROCHE shall reimburse INSTITUTION for all reasonable expenses incurred thereby and such expenses shall be considered advances against future royalties under the subject license agreement between the parties.

8. Confidentiality. Because INSTITUTION and ROCHE will be cooperating with each other in this evaluation and because each may reveal to the other in the course of this evaluation certain confidential information, INSTITUTION and ROCHE agree to hold as proprietary or confidential information: i) any and all information, data, know-how, whether written or oral, technical or non-technical, as well as tangible materials, including without limitation samples, models, drawings, or diagrams belonging to the other party which is obtained during the course of this study and ii) any other data or information resulting from the study which is not authorized by ROCHE for publication as provided in Section 9, Publication Rights (hereinafter "Confidential Information"). Neither party shall disclose the Confidential Information to any third party without the express written consent of the other party to this Agreement. This requirement shall remain in force for a period of four (4) years following completion of work under this Agreement. Nothing in this paragraph shall in any way restrict the rights of either INSTITUTION or ROCHE to use, disclose or otherwise deal with any information which:

(a) Can be demonstrated to have been in the public domain as of the effective date of this Agreement or which subsequently enters the public domain through no act of the recipient;

(b) Can be demonstrated by written records to have been known to recipient at the time of disclosure by the disclosing party;

(c) Can be demonstrated to have been rightfully received by the recipient after disclosure under this Agreement from a third party who did not require the recipient to hold it in confidence or limit its use and who did not acquire it, directly or indirectly, from the other party to this Agreement under a continuing obligation of confidentiality;

(d) Shall be required for disclosure to Federal regulatory agencies pursuant to a request for approval for use or to file patent applications related to any inventions conceived, developed, or reduced to practice under this Agreement; or

(e) Can be demonstrated by adequate written evidence to the disclosing party to have been independently derived by another investigator of the recipient party not involved in the performance of work under this Agreement, which in the case of the INSTITUTION shall include component institutions of the University of Texas System.

Except as provided in Article 9 below, the raw data or other information which results from the study shall be deemed confidential and proprietary information of ROCHE.

**{IF YOUR STUDY IS MULTI-CENTER, USE PARAGRAPHS 9.(A), (B) AND (C). IF YOUR STUDY IS NOT MULTI-CENTER, USE THE ALTERNATIVE PARAGRAPHS (a) and (b). IN EITHER CASE DELETE THE PARAGRAPHS YOU DO NOT USE}**

9. Publication Rights.

(A) INSTITUTION acknowledges that the study is part of a multi-center study, and that an independent, joint publication is anticipated to be authored by investigators in the multi-center study, including INSTITUTION's investigator. Therefore, INSTITUTION agrees not to independently publish the results of the study before the publication of the multi-investigator paper; but in no event shall INSTITUTION be so restricted after the expiration of two (2) years from completion of INSTITUTION's performance of the study.

(B) ROCHE shall complete its review within thirty (30) working days after receipt of the Proposed Publication by INSTITUTION. If ROCHE believes that any Proposed Publication contains any information relating to patentable items, the disclosure of such Proposed Publication to any third party shall be delayed for up to six (6) months to permit the filing of a patent application. Should ROCHE request such a delay, then upon the written request of INSTITUTION, ROCHE shall, consistent with reasonable business and scientific practice, expedite the filing of such patent application. If ROCHE believes that any Proposed Publication contains any Confidential Information, ROCHE shall have the right to remove the references to such Confidential Information.

(C) Notwithstanding the foregoing, INSTITUTION shall not issue a press release that references the study or its results, or that uses ROCHE's name or trademarks without the express written consent of ROCHE.

**{OR}**

(a) Institution reserves the right to publish the results of the Study, with due regard for the protection of ROCHE's confidential information. Institution will submit the manuscript of any proposed publication to ROCHE at least thirty (30) days before publication, and ROCHE shall have the right to review and comment upon the publication in order to protect ROCHE's confidential information. Upon ROCHE's request, publication will be delayed up to sixty (60) additional days to enable ROCHE to secure adequate intellectual property protection of property of ROCHE that would be affected by said publication.

(b) Institution acknowledges, however, that the Study is part of a multi-center study, and that a non-independent, joint publication is anticipated to be authored by ROCHE and the investigators in the multi-center study, including Institution's investigator, in accordance with the provisions of the "Statement of Publication Policy" attached hereto as Exhibit II. Therefore, Institution agrees not to independently publish the results of the Study before the publication of the first multi-investigator paper; but in no event shall Institution be restricted in any manner whatsoever by the terms and conditions of Exhibit II after the expiration of eighteen (18) months from completion of Institution's performance of the Study.

10. Publicity. INSTITUTION acknowledges ROCHE's intention to distribute periodically information releases and announcements to the news media regarding the progress or research hereunder. ROCHE shall not release such materials containing the name of INSTITUTION or any of its employees without prior written approval by an authorized representative of INSTITUTION. Should INSTITUTION reject the news release, INSTITUTION and ROCHE agree to discuss the reasons for INSTITUTION's rejection, and every effort shall be made to develop an appropriate informational news release within the bounds of accepted academic practices. ROCHE reserves the same right in the event that INSTITUTION desires to distribute a news release concerning the research program. Nothing herein shall be construed as prohibiting INSTITUTION or ROCHE from reporting on this study to a governmental agency or otherwise identifying the study as required by law.

11. Responsibility. Not in any limitation of the provisions of Article 16, the parties each agree to assume individual responsibility for the actions and omissions of their respective employees, agents and assigns in conjunction with this evaluation.

12. Independent Contractor. ROCHE will not have the right to direct or control the activities of INSTITUTION in performing the services provided herein, INSTITUTION shall perform services hereunder only as an independent contractor, and nothing herein contained shall be construed to be inconsistent with that relationship or status. Under no circumstances shall INSTITUTION be considered to be an employee or agent of ROCHE. This Agreement shall not constitute, create or in any way be interpreted as a joint venture, partnership or formal business organization of any kind.

13. Title to Equipment. INSTITUTION shall retain title to all equipment purchased and/or fabricated by it with funds provided by ROCHE under this Agreement.

14. Survivorship. The provisions of Articles 7, 8, 9, 10, 14 and 16 hereof shall survive any expiration or termination of this Agreement.

15. Assignment. This Agreement may not be assigned by either party without the prior written consent of the other party; provided, however, that ROCHE may assign this Agreement to an affiliate (which does not include joint venturers, licensees or sublicensees of ROCHE) or any purchaser or transferee of all or substantially all of ROCHE's business upon prior written notice to INSTITUTION.

16. Indemnification. ROCHE agrees to indemnify and hold harmless INSTITUTION, System, their regents, officers, agents and employees (the "Indemnified Parties") from any liability, loss or damage they may suffer as a result of claims, demands, costs or judgments against them arising out of the performance of this Agreement in accordance with the Protocol, including but not limited to the use by ROCHE of the results thereof (the "Claims"), provided, however, that any such liability, loss, or damage resulting from the following Subsections "a", "b" or "c" is excluded from this Agreement to indemnify and hold harmless:

(a) a failure to comply with any applicable FDA or other governmental requirements; or

(b) the negligence or willful malfeasance by any regent, officer, agent or employee of INSTITUTION or System; or

(c) the failure to adhere to the terms of the Protocol or ROCHE's written instructions relative to the use of the compound, except for minor technical deviations from the Protocol that do not give rise to any Claims.

It is, however, understood and agreed that the above provision is only for purposes of this indemnification and does not authorize any deviation whatsoever from the Protocol without the express written consent of ROCHE and INSTITUTION's Institutional Review Board ("IRB") unless such deviation is immediately necessary to protect the health of a study subject. It is further understood that certain Protocol deviations, excluding that set forth in the preceding sentence, may invalidate the entire study. In the event of a Protocol deviation that is shown to have invalidated the study as a pivotal study for approval of the Compound by the Food and Drug Administration, INSTITUTION agrees to reimburse ROCHE for all payments made under this Agreement.

All such Claims described above for which ROCHE is solely obligated to provide indemnification and is solely obligated to provide a defense hereunder shall be hereinafter referred to as "Indemnified Claims."

Both parties agree that the party receiving the notice of any Claims will promptly notify the other party. Subject to the statutory duties of the Texas Attorney General, ROCHE at its own expense will carry out the sole management and defense of the Indemnified Claims, and shall provide attorneys of its sole choosing to defend against the Indemnified Claims. The Indemnified Parties at their own expense will carry out the sole management and defense of all other claims (the "Non-Indemnified Claims"), and shall provide attorneys of their sole choosing to defend against the Non-Indemnified Claims. ROCHE shall not be obligated to indemnify with respect to Non-Indemnified Claims. In the event any lawsuit or other action is instituted which alleges both Indemnified Claims and Non-indemnified Claims, the parties shall cooperate with each other unless a conflict of interest develops, in which event the parties shall maintain separate management and defense of the Indemnified Claims (in the case of ROCHE), and the Non-Indemnified Claims (in the case of the Indemnified Parties). In the event any lawsuit or other action is instituted which alleges only Indemnified Claims, the Indemnified Parties shall cooperate with ROCHE in the defense of the Indemnified Claims. In the event ROCHE is prohibited from carrying out the sole management and defense of any Indemnified Claims under any applicable law, ROCHE shall have no obligation to defend or indemnify the Indemnified Parties unless ROCHE has given its written consent to provide indemnification prior to any disposition, judgment or settlement of such Indemnified Claims. In no event shall this Agreement operate to eliminate either ROCHE's or the Indemnified Parties' right to common law indemnification, contribution or apportionment.

It is further understood and agreed as between ROCHE and INSTITUTION that the above agreement to indemnify is not intended as or for a substitute for full and complete malpractice and other forms of liability insurance and that INSTITUTION shall obtain any insurance coverage necessary and proper for the regular conduct of such activities.

17. Award. ROCHE agrees to pay INSTITUTION a fee of and No/100 Dollars ($ .00) for study expenses for the clinical study of ( ) patients. This fee shall be payable in four (4) equal installments, payable as follows:

(a) $ .00 within thirty (30) days after the effective date of this Agreement;.

(b) $ .00 upon INSTITUTION's Entry (as defined below) of one-third (1/3) of the research subjects;

(c) $ .00 upon INSTITUTION's Entry of two-thirds (2/3) of the research subjects; and

(d) $ .00 upon ROCHE's receipt of all the completed evaluable case reports and the final report in accordance with the Protocol.

As used above, "Entry" shall refer to the fulfillment of all pre-study eligibility criteria, randomization and entry into the study as defined in the attached Protocol.

An estimate of INSTITUTION's expenses in connection with the study is attached as Exhibit II to this Agreement for informational purposes only. Payment as set forth in this Section shall constitute full payment for the study and ROCHE shall have no other payment obligations hereunder.

18. Term and Termination. This Agreement shall become effective as of the date first hereinabove written and, unless earlier terminated as hereinafter provided, shall continue in force until ROCHE receives all completed case reports and the final report. INSTITUTION shall complete the study by \_\_\_\_\_\_\_\_\_. Either party may terminate this Agreement upon sixty (60) days prior written notice to the other party.

Upon the termination of this Agreement by INSTITUTION before the end of the term, the except where INSTITUTION has terminated this Agreement because of default by ROCHE, the total payable by ROCHE under this Agreement shall be $2,500.00 per completed evaluable case report in accordance with the Protocol received by ROCHE. Upon the termination of this Agreement before the end of the term for any other reason, the total payable by ROCHE under this Agreement shall be equal to the non-cancelable expenses incurred by INSTITUTION in the performance of this Agreement until either the termination date or the receipt of notice of termination, whichever is earlier.

19. Default. If either party to this Agreement breaches any material provisions hereof, the party complaining of said breach shall give the breaching party written notice of the breach and thirty (30) days to cure said breach before this Agreement is affected in any way. Should either party fail to cure its breach within thirty (30) days after receipt of written notice thereof, or such extended time as the complaining party may grant in writing, the complaining party may terminate this Agreement by written notice to the other party, notwithstanding anything to the contrary contained in this Agreement.

20. Entire Agreement. The parties acknowledge that this Agreement represents the sole and entire understanding between the parties hereto pertaining to the evaluation of the Compound and that such supersedes all prior agreements, understandings, negotiations, and discussion regarding the same, whether oral or written. There are no warranties, representations or other agreements between the parties in connection with the subject matter hereof except as specifically set forth herein. No supplement, amendment, alteration, modification, waiver or termination of this Agreement shall be binding unless executed in writing by the parties hereto.

21. Reform of Agreement. If any provision of this Agreement is, becomes, or is deemed invalid, illegal, or unenforceable in any court of competent jurisdiction, such provisions shall be deemed amended to conform to applicable laws so as to be valid and enforceable; or (with the exception of Articles 3, 8, 16, and 17,) if it cannot be so amended without materially altering the intention of the parties, it shall be stricken, and the remainder of this Agreement shall remain in full force and effect.

22. Captions. The captions in this Agreement are for convenience only and shall not be considered a part of or affect the construction or interpretation of any provision of this Agreement.

23. Notices. Any notices required by this Agreement shall be sent by certified mail, postage prepaid and addressed as follows:

If to INSTITUTION:

The University of Texas \_\_\_\_\_\_\_
\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

If to ROCHE:

Hoffmann-La Roche, Inc.
340 Kingsland Street, Bldg. 719
Nutley, New Jersey 07110

All medical/scientific communications, statements and reports shall be considered given if sent postage prepaid to the Principal Investigator. All legal notices by either party required by this Agreement shall be in writing and shall be sent by registered or certified mail, return receipt requested, with all postage prepaid to the above address, and, in the case of ROCHE with a copy to the Corporate Secretary, and, in the case of INSTITUTION with a copy to\_\_\_\_\_\_\_\_\_ . Such notices shall be considered effective upon receipt. All notices concerning the exercise of intellectual property options shall be additionally sent to The University of Texas System, Intellectual Property Office, Office of General Counsel, 201 West 7th Street, Austin, Texas 78701.

24. Conflicts. Any conflicts between the Protocol and this Agreement shall be controlled by this Agreement.

25. Debarment. INSTITUTION represents that it has never been and, to the best of its knowledge after reasonable inquiry, its employees have never been 1) debarred, or 2) convicted for a crime for which a person can be debarred, under section 335a (a) or (b) of the Generic Drug Enforcement Act of 1992 ("Section 335a (a) or (b)"). INSTITUTION represents that it has never been and, to the best of its knowledge after reasonable inquiry, none of its employees have ever been 1) threatened to be debarred, or 2) indicted for a crime or otherwise engaged in conduct for which a person can be debarred under Section 335a (a) or (b). INSTITUTION agrees that it will promptly notify ROCHE in the event of any such debarment, conviction, threat or indictment of either INSTITUTION or INSTITUTION's employees. The terms of the preceding sentence shall survive the termination or expiration of this Agreement for a period of three (3) years. Notwithstanding the provisions of Paragraph 18 of this Agreement, INSTITUTION acknowledges that ROCHE shall have the right to terminate this Agreement immediately upon receipt of information regarding the debarment, conviction, threat or indictment of either INSTITUTION or INSTITUTION's employees.

IN WITNESS WHEREOF, INSTITUTION and ROCHE have entered into this Agreement effective as of the date first hereinabove written and have executed two (2) duplicate originals each of which are of equal dignity.

|  |  |
| --- | --- |
| University of Texas \_\_\_\_\_\_\_\_\_\_\_\_ By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_                                Name Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  | Hoffman-LaRoche, Inc. By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_                                Name Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  |

PRINCIPAL INVESTIGATOR'S CERTIFICATION:

I acknowledge that I have read this Agreement and I understand my obligations hereunder.

I certify that I have not been delisted by the federal Food and Drug Administration or otherwise disqualified from serving as a Principal Investigator.

I certify that I have not been debarred under the provisions of the Generic Drug Enforcement Act of 1992, 21 U.S.C. §335a (a) and (b). In the event that I become debarred, I shall immediately cease all activities relating to this Agreement and promptly notify the INSTITUTION.

By: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
        Principal Investigator

Mail payments to:

The University of Texas
\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
Tax I.D.: 74-6001118-A1

EXHIBIT II

CLINICAL STUDY AGREEMENT

BETWEEN

THE UNIVERSITY OF TEXAS

AND

HOFFMANN-La ROCHE, INC.

"\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ "

The approximate distribution of expenses related to the study described in the covering Agreement is as follows:

|  |  |
| --- | --- |
| Salaries (including fringe benefits) Supplies Data Management CostsPharmacy CostsIndirect Costs (institutional overhead)                                                  TOTAL  | $ .00 $ .00$ .00$ .00$ .00$ .00  |

Such expenses are provided for information only. INSTITUTION reserves the right to modify the distribution of such expenses as necessary in the circumstances, provided that the stipulated total cost of $.00 and the line item for total indirect overhead cost of $.00 are not exceeded.

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